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Health Hazard Assessment Summary
Steel Mill Emissions

Radian Corp., Research Triangle Park, NC

Prepared for:

Environmental Protection Agency, Research Triangle Park, NC

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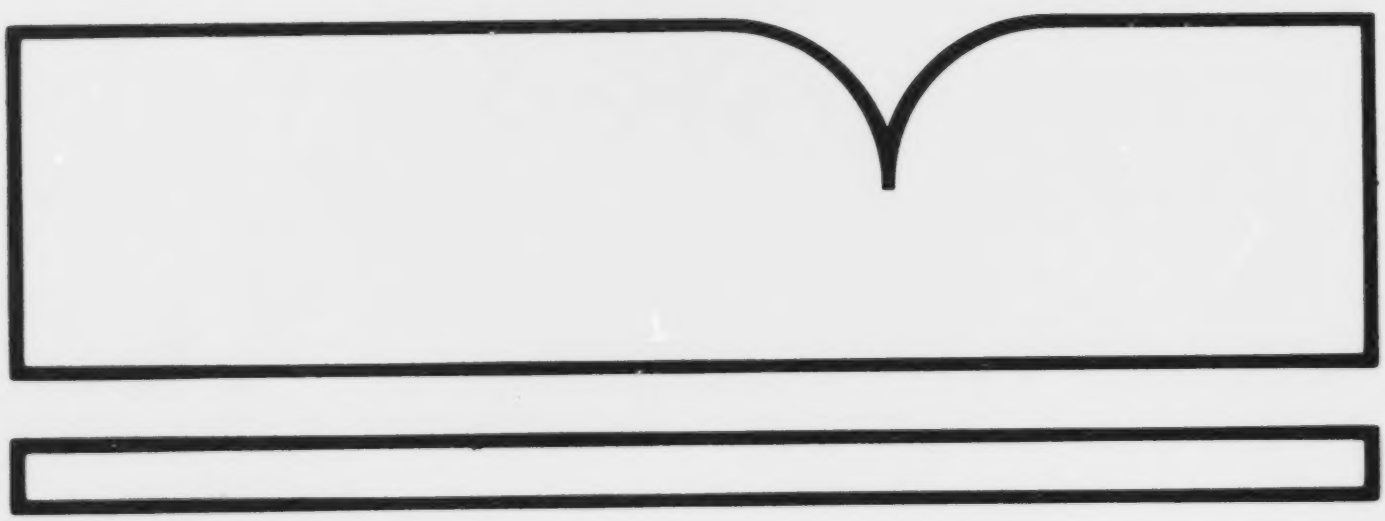

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HEALTH HAZARD ASSESSMENT SUMMARY: STEEL MILL EMISSIONS

Work Assignment 07

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Emission Standards Division
Pollutant Assessment Branch
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September 29, 1989

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This report has been reviewed by the Office of Air Quality Planning and Standards and the Environmental Criteria and Assessment Office of the Office of Health and Environmental Assessment, United States Environmental Protection Agency, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policy of the United States Environmental Protection Agency, nor does the mention of trade or commercial products constitute endorsement or recommendations for use.

PREFACE

This report has been prepared for the Air Risk Information Support Center (Air RISC) which is a cooperative endeavor between the Office of Air Quality Planning and Standards (OAQPS) and the Office of Health and Environmental Assessment (OHEA), U.S. Environmental Protection Agency (EPA). The purpose of the Air RISC is to provide technical support to EPA Regional Offices and State and local air pollution control agencies on matters pertaining to health, exposure and risk assessment. This report contains information residing in EPA's Integrated Risk Information System (IRIS) and is current as of September 1989. The IRIS is a computer-based compilation of pollutant health effect information and is subject to frequent updates. The reader should note that information such as reference doses or concentrations, lowest adverse effect levels and no effect levels may have been changed since publication of this report. For more information on how to access IRIS, contact IRIS User Support, Environmental Criteria and Assessment Office, U. S. EPA, 26 W. Martin Luther King Drive, Cincinnati, OH 45268, telephone 513-569-7254.

TABLE OF CONTENTS

Section			Page
1.0	INTRODUCTION		1
2.0	HEALTH EFFECTS OF METALS EMITTED FROM STEEL MILLS		4
	2.1	Chromium	4
		2.1.1 Noncancer Health Effects	4
		2.1.2 Carcinogenicity of Chromium	5
		2.1.2 Interaction with Other Compounds	7
	2.2	Manganese	7
		2.2.1 Noncancer Health Effects	7
		2.2.2 Carcinogenicity of Manganese	10
		2.2.3 Interaction with Other Compounds	11
	2.3	Zinc	11
		2.3.1 Noncancer Health Effects	11
		2.3.2 Carcinogenicity of Zinc	12
		2.3.3 Interaction with Other Compounds	12
	2.4	Copper	13
		2.4.1 Noncancer Health Effects	13
		2.4.2 Carcinogenicity of Copper	14
	2.5	Nickel	15
		2.5.1 Noncancer Health Effects	15
		2.5.2 Carcinogenicity of Nickel	16
		2.5.3 Interaction with Other Compounds	17
		2.5.4 Populations at Risk	17
	2.6	Cadmium	17

Table of Contents Continued

Section		Page
	2.6.1 Noncancer Health Effects	18
	2.6.2 Carcinogenicity of Cadmium	19
	2.6.3 Interaction with Other Compounds	20
	2.6.4 Populations at Risk	20
2.7	Vanadium	20
	2.7.1 Noncancer Health Effects	21
	2.7.2 Carcinogenicity of Vanadium	22
	2.7.3 Interaction with Other Compounds	22
3.0	HEALTH EFFECTS OF OTHER COMPOUNDS EMITTED FROM STEEL MILLS	23
3.1	Ammonia and Ammonium sulfate	23
	3.1.1 Noncancer Health Effects	23
	3.1.2 Carcinogenicity of Ammonia and Ammonium Sulfate	25
	3.1.3 Interaction with Other Compounds	25
3.2	Hydrogen chloride	25
	3.2.1 Noncancer Health Effects	26
	3.2.2 Carcinogenicity of Hydrogen chloride	26
3.3	Toluene	26
	3.3.1 Noncancer Health Effects	27
	3.3.2 Carcinogenicity of Toluene	28
3.4	Benzene	28
	3.4.1 Noncancer Health Effects	28
	3.4.2 Carcinogenicity of Benzene	29

Table of Contents Continued

Section		Page
3.4.3	Interaction with Other Compounds	29
3.5	Naphthalene	30
3.5.1	Noncancer Health Effects	30
3.5.2	Carcinogenicity of Naphthalene	31
4.0	HEALTH EFFECTS OF COMPLEX MIXTURES	32
4.1	Polycyclic Organic Matter	32
4.1.1	Noncancer Health Effects	32
4.1.2	Carcinogenicity of Polycyclic Organic Matter	34
4.2	Coke Oven Emissions	34
4.2.1	Noncancer Health Effects	35
4.2.2	Carcinogenicity of Coke Oven Emissions	36
5.0	REFERENCES	38

LIST OF TABLES

Table		Page
1.	Substances of Concern Potentially Emitted from Steel Mills	2

1.0 INTRODUCTION

The U. S. Environmental Protection Agency's (EPA) Air Risk Information Support Center (Air RISC) was developed and is maintained by the Pollutant Assessment Branch of the Office of Air Quality Planning and Standards (PAB/OAQPS) and the Environmental Criteria and Assessment Office of the Office of Health and Environmental Assessment (ECAO/OHEA) to assist State and local air pollution control agencies and EPA regional offices on technical matters pertaining to toxic air pollutants. In response to an Air RISC request on the public health hazards associated with steel mill emissions, this document was prepared to assist State and local air pollution control officials in the identification of possible health hazards, and can be used with its companion document, "Emission Factors For Iron and Steel Sources/Criteria and Toxic Pollutants" (Barnard, 1989) to quantify steel mill emissions and assess the health impacts on affected populations.

The majority of the information presented in this assessment is derived from summary documents prepared by the EPA for the specific compounds shown in Table 1. These compounds have been identified in steel mill emissions by Barnard (1989). When information was available for a mixture of compounds known to be emitted during steel production, the discussion considers the mixture as a whole rather than the individual chemicals. This is the case for polycyclic organic matter and coke oven emissions (see Section 4).

One of the objectives of this document is to present the Lowest Observed Effect Levels (LOEL) (or Lowest Observed Adverse Effect Levels) and the No Observed Effect Levels (NOEL) (or the No Observed Adverse Effect Levels) for the noncancer health effects associated with exposure to steel mill emissions. The LOEL and the NOEL presented here are derived from the EPA's reviews of

animal toxicity and human epidemiology studies, and it is possible that further research may find an alternate NOEL or LOEL.

For some pollutants, the "critical" study or effect for a NOEL or a LOEL has been identified by the EPA and used to calculate a Reference Dose (RfD). An RfD is defined as an estimate (within uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive sub-populations) that is likely to be without deleterious effects during a lifetime. When the RfD is reported in units of milligrams of substance per cubic meter of air breathed it is designated an Inhalation Reference Dose (RfD_i). If an RfD_i has been verified from the substance it can be found in the EPA's Integrated Risk Information System (IRIS), a computer-

Table 1. Substances of Concern Potentially Emitted from Steel Mills

Chromium
Manganese
Zinc
Copper
Nickel
Cadmium
Vanadium
Ammonia/Ammonium sulfate
Hydrogen chloride
Toluene
Benzene
Naphthalene
Polycyclic organic matter
Coke oven emissions

based compilation of pollutant health effects information. For additional information on IRIS, contact IRIS User Support, Environmental Criteria and Assessment Office, U. S. EPA, 26 W. Martin Luther King Drive, Cincinnati, OH 45268, telephone 513-569-7254.

Information is also presented here on the carcinogenic potential of steel mill emissions. This information was also derived from EPA documents and IRIS. The EPA's Human Health Assessment Group has calculated unit risk estimates for several of the compounds discussed in this document. The incremental unit risk estimate for an air pollutant is defined as the additional lifetime cancer risk for a given population exposed continuously for their lifetimes (70 years) to a concentration of 1 ug/m^3 of an airborne pollutant (U. S. EPA, 1986a). These unit risk estimates are then used to compare the carcinogenic potency between air pollutants and to help give an estimate of the population risk that might be associated with exposures to air or water that contains the carcinogenic substance. The data used to calculate these unit risk numbers come either from lifetime animal studies or human epidemiological studies. The EPA also assigns a weight-of-evidence judgment of the likelihood that an agent is a human carcinogen (U.S. EPA, 1989). The Integrated Risk Information System also includes an estimation of the air concentrations expected to result in 1 in 10,000; 1 in 100,000; and 1 in 1,000,000 risk.

Finally, it should be noted that, for some of the compounds discussed in this document, little or no information is available concerning their effects from chronic inhalation exposure. For these compounds, acute inhalation studies are summarized to provide some indication of their potential toxicity. Oral exposures may also be discussed, but it must be kept in mind that route-to-route extrapolation for some effects may be inappropriate.

2.0 HEALTH EFFECTS OF METALS EMITTED FROM STEEL MILLS

2.1 CHROMIUM

Chromium is a naturally occurring essential element that can also be carcinogenic (U. S. EPA, 1984a). Chromium can be present in the atmosphere in several valence states, but this discussion will center on the two valence states that humans are most likely to encounter. Trivalent chromium [Cr (III)] and hexavalent chromium [Cr (VI)] are the two most stable forms of chromium (U. S. EPA, 1984a). Chromium (III) is emitted naturally from the earth's crust. Chromium (VI) is readily reduced to Cr (III) in the presence of organic matter, but is emitted from anthropogenic sources such as steel mills (U. S. EPA, 1984a). Steel mills are one source category thought to emit both Cr (III) and Cr (VI) but the relative proportions are unknown (U. S. EPA, 1984a).

Because the mineral chromite occurs naturally, chromium can be taken into the body through air, food, and water exposures. All of these exposure routes must be taken into consideration in making an estimate of total chromium uptake.

2.1.1 Noncancer Health Effects

Epidemiologic studies by Bloomfield and Blum (1928), Langard and Norseth (1979), Seeber et al. (1976), Lindberg and Hedenstierna (1983), and others reviewed by the World Health Organization (WHO, 1988) and the Agency for Toxic Substances and Disease Registry (ATSDR, 1989) indicate that perforation of the nasal septum is the critical noncancer health effect associated with chronic, low-level exposure to chromium (VI). Lindberg and Hedenstierna (1983) studied workers in the chrome plating industry who were exposed to "low" chromic acid

concentrations (8-hour mean below 2 ug/m^3) and "high" chromic acid concentrations (above 2 ug/m^3) for an average exposure time of 2.5 years. Lindberg and Hedenstierna (1983) also studied lung function in chrome plating workers, and reported that an 8-hour mean exposure level of more than 2 ug/m^3 might cause a transient decrease in lung function (WHO, 1988).

On the basis of this study, the World Health Organization (1988) concluded that long term exposure to doses greater than 1 ug chromium (VI) can cause nasal irritation, atrophy of the nasal mucosa, and ulceration or perforation of the nasal septum. This concentration can be considered to be the unadjusted NOEL for exposure to chromic acid, and 2 ug/m^3 can be considered the LOEL.

The effects of chromium have been studied in animal experiments, with the chronic studies primarily evaluating chromium's carcinogenic potential. These experiments are discussed below, and support the finding of carcinogenicity seen in human occupational studies.

2.1.2 Carcinogenicity of Chromium

Animal studies have not shown lung cancer resulting from chromium inhalation exposures, but epidemiologic studies of several chromate production facilities have shown an association between chromium exposure among workers and lung cancer. Epidemiology studies conducted in the chrome pigment industry and the chromium plating industry also have shown an association between lung cancer and exposure to chromium (Mancuso, 1975; Langard et al., 1980; Axelsson et al., 1980; and Pokrovskaya and Shabynina, 1973) as cited in U.S. EPA (1989). These exposures have been to both Cr (III) and Cr (VI), but animal studies suggest that Cr (VI) rather than Cr (III) causes cancer

following exposure via other routes (U.S. EPA, 1989), thus implicating Cr (VI) as the carcinogenic form of chromium. Research is currently underway to elucidate the issue. Because of the excess cancers seen in chromate production facilities, chromium (VI) is considered by the EPA's Human Health Assessment Group (HHAG) to have sufficient evidence for designation as a human carcinogen. Epidemiologic evidence has been derived from studies in the United States, Great Britain, Japan, and West Germany.

The HHAG estimated a unit risk number based on the epidemiologic studies of Mancuso (1975), Langard et al. (1980), Axelsson et al. (1980), and Pokrovskaya and Shabynina (1973). The Human Health Assessment Group thus calculated a unit risk number of $1.2 \times 10^{-2}/ug/m^3$. This means that if a person continuously breathes 1 ug/m^3 of Cr (VI) for 70 years, the probability of getting lung cancer would not exceed 1.2 chances in 100. The Integrated Risk Information System presents the carcinogenic risk levels for chromium (VI), showing a conservative estimate of lung cancer risk of 1 in 10,000 for a population exposed continuously to 0.008 ug/m^3 Cr(VI) for 70 years.

As mentioned previously, lung cancer has not been observed in animal assays with Cr (VI). The HHAG's review of the supporting data for carcinogenicity comes from animal assays in which intramuscular injection site tumors were seen (Furst et al, 1976; Maltoni, 1974, 1976; Payne, 1960; Hueper and Payne, 1959), as cited in U.S. EPA (1989). In addition, intrapleural implant site tumors, intrabronchial implantation site tumors, and subcutaneous injection site sarcomas have been seen in rats in several studies.

On the basis of the human and animal studies, chromium (VI) is considered by the EPA to be a Group A carcinogen, with sufficient evidence as

a human carcinogen and sufficient evidence as an animal carcinogen (U.S. EPA, 1989).

2.1.3 Interaction with Other Compounds

Chromium's carcinogenicity has been tested in laboratory animals preexposed with virus infections, ionizing radiation, and 20-methylcholanthrene, another known carcinogen (Nettesheim et al., 1970, 1971; Steffee and Baetjer, 1965; Shimkin and Leiter, 1940). No synergism was detected in any of the experiments (WHO, 1988).

2.2 MANGANESE

Manganese, like chromium, is present in the earth's crust and is released to the atmosphere through entrainment of road dusts, wind erosion, soil disturbances through farming and construction activities, combustion, and the manufacture of ferroalloys, iron and steel, batteries, and chemical products (U. S. EPA, 1984b). Exposure can occur from contact with food, water, and air that contains either naturally occurring or anthropogenically released manganese. Manganese-containing particles released during the steel manufacturing process are submicron in size, ranging from 0.5 to 5.0 um mass median diameter (U. S. EPA, 1971). Manganese is emitted in the form of the metal, as trimanganese tetraoxide (Mn_3O_4), and as manganese oxide (MnO) during steel manufacture (U. S. EPA, 1971).

2.2.1 Noncancer Health Effects

Following exposure to manganese particles, deposition is dependent upon the mass median diameter of the inhaled particles. According to the Environmental Protection Agency (1984b), 25 to 65% of the particles between 2 and 4 um are deposited in the alveoli of the lungs, with the remainder

deposited in the tracheobronchial region. Nearly all of the particles smaller than 2 um are deposited in the alveoli. Particles less than 1 um are likely to be adsorbed directly into the blood (Task Group on Metal Accumulation, 1973), and the GI tract is the portal of entry for the larger particles (Mena et al., 1969).

Although manganese has been shown to be necessary for normal growth and reproduction in laboratory animals, there is no minimum daily requirement for humans, and no human studies have demonstrated a manganese deficiency.

Chronic occupational exposures to manganese concentrations above 300 ug/m^3 often result in manganism, which predominantly affects the central nervous system. The symptoms of manganism range from anorexia, insomnia, and abnormal behavior to severe rigidity, tremors, and autonomic dysfunction (U. S. EPA, 1984b).

The U.S. Environmental Protection Agency (1984b) examined over ten epidemiologic studies of workers exposed to several chemical forms of manganese and particle sizes to determine a NOEL for manganism (Flinn et al., 1941; Ansola et al., 1944a,b; Rodier, 1955; Schuler et al., 1957; Tanaka and Lieben, 1969; Emara et al., 1971; Smyth et al., 1973; Suzuki et al., 1973a,b; Saric et al., 1977; Chandra et al., 1981). The occupations examined were ore crushing, mining, general industrial, dry-cell battery production, ferromanganese production, and welding. From review of these studies, the EPA concluded that the dose-response information was insufficient to establish the NOEL, but that enough information was available to estimate a LOEL.

Ansola et al. (1944b) and Rodier (1955) concluded that manganism can develop after a few months of occupational exposure, but most cases are seen

following several years of exposure. The EPA found that the data identifying a LOEL below 0.3 mg/m^3 (300 ug/m^3) were equivocal or inadequate, but the duration of exposure to this level was not stated, and the chemical form and the particle sizes of the manganese were not reported in the original studies. However, the study by Saric et al. (1977) of ferromanganese plant dust and fumes estimated the duration of exposure to be less than 4 years for 27% of the study population. A NOEL could not be established because of an inability to evaluate the early stages of the disease (U. S. EPA, 1984b).

Bronchitis and pneumonitis are the primary pulmonary effects of manganese, but these effects are thought to be due to particulate matter in general, rather than manganese specifically (U. S. EPA, 1984b). Pulmonary effects below 1 mg/m^3 are generally reversible. Several reports suggested a relationship between manganese levels and the rate of pneumonia and other respiratory ailments in populations living near sources of manganese. The lowest exposure level where pulmonary effects occurred was reported in a study of junior high school students exposed to emissions from a ferromanganese plant in Japan. Nogawa et. al. (1973) studied school children who lived from 50 to 1500 meters from the plant and attended a school that was 100 meters from the plant. They found a relationship between the distance of the children's homes and the plant, with those closest to the plant showing a higher number of cases of "throat swelling and soreness in summer" and a "past history of pneumonia" (Nogawa et al., 1973). They estimated that more than 1500 meters from the plant, manganese concentrations were negligible, and 300 meters from the plant suspended dust and manganese concentrations were 160 ug/m^3 and 6.7 ug/m^3, respectively (Nogawa et al., 1973). Other measurements

100 meters from the plant indicated dust levels of 299 ug/m^3 and manganese levels of 4 ug/m^3. The U. S. Environmental Protection Agency (1984b) concluded on the basis of this study that the LOAEL for pulmonary effects for exposure to manganese-containing particulate matter is 3-11 ug/m^3.

Based on the high incidence of pneumonia or other acute respiratory diseases in many occupational studies (Heine, 1943; Rodier, 1955; Cauvin, 1943; Lloyd-Davies, 1946), the EPA (1984b) concluded that manganese-containing particulate matter may disturb normal lung clearance mechanisms, thus increasing susceptibility. Animal studies have been undertaken to investigate this possibility. Several investigators found that manganese had an effect on the number and phagocytic activity of alveolar macrophages. Ulrich et al. (1979a,b,c) found no pulmonary effects, however, in rats and monkeys exposed to 0.113 mg/m^3 (113 ug/m^3) Mn_3O_4 for 24 hours/day for 9 months, and the EPA concluded that this level was the highest available animal NOEL. Suzuki et al. (1978) found positive radiologic findings in monkeys exposed for 10 months (22 hours/day) to 0.7 mg/m^3 MnO_2, and the EPA considers this to be the animal LOAEL.

2.2.2 Carcinogenicity of Manganese

The U. S. EPA's review of manganese carcinogenicity studies is presented in IRIS (1989). No evidence exists in the epidemiology studies to support a claim that manganese is carcinogenic, and the animal data are considered to be inadequate by the EPA's HHAG. The weight-of-evidence classification for manganese is that it is a group D compound, not classifiable as to human carcinogenicity.

2.2.3 Interaction with Other Compounds

Populations at risk for manganese exposure are those with iron deficiencies, as an iron deficiency may exacerbate manganese toxicity (Thomson et al., 1971). Manganese has also been shown to inhibit local sarcoma induction by benzo(a)pyrene (U. S. EPA, 1984b).

2.3 ZINC

Zinc is found in nature in its salt or oxide form and does not occur naturally in its elemental form (U. S. EPA, 1987a). Elemental zinc is, however, used extensively in the galvanizing of iron and steel. Exposure to zinc may occur via inhalation and ingestion of food and water.

2.3.1 Noncancer Health Effects

The form in which zinc is emitted from steel mills is not known, therefore the health effects presented here pertain to elemental zinc and zinc oxide. The primary health effect observed in the occupational settings is "metal fume fever." It has been reported that this condition exists at zinc oxide concentrations greater than 15 mg/m^3 (Batchelor et al., 1926; Kemper and Troutman, 1972; Hammond, 1944). Symptoms associated with metal fume fever are headache, fever, hyperpnea, nausea, sweating, and muscle pain. Metal fume fever symptoms tend to recur at the beginning of the work week (U. S. EPA, 1987a).

One epidemiologic study has shown that exposure to zinc oxide (0.2 to 5.1 mg/m^3) over a 5 year period resulted in increased respiratory effects (Bobrishchev-Pushkin et al., 1977). These effects included chronic bronchitis and diffuse pneumosclerosis. In another epidemiologic study, Batchelor et al., (1926) found slight leukocytosis in 14 of 24 workers at a zinc smelter in

New Jersey. The smelter workers were exposed to elemental zinc in concentrations ranging from 35 to 130 mg/m^3.

The effects of zinc have been studied in animals to determine its subchronic toxicity. Pistorius (1976) investigated the effects of inhalation of zinc oxide particles (less than 1 micron in size) on rat lungs. The only differences noted in lung function between the controls and exposed animals were a decrease in specific conductance and difference volume in the exposed group given 15 mg/m^3 zinc oxide for 1, 4, or 8 hours/day for 84 days. In another study Pistorius et al. (1976) examined the effect of zinc oxide dust administered to rats for 4 hours/day, 5 days/week for 1, 14, 28, and 56 days. Histological examination showed leukocytic inflammatory changes and fluid in the alveolar region. These inflammatory changes decreased by days 28 and 56.

On the basis of the above epidemiologic and animal studies, the unadjusted LOEL for zinc oxide is 0.2 mg/m^3 for humans and 15 mg/m^3 in laboratory animals. No data were found from which a NOEL could be determined.

2.3.2 Carcinogenicity of Zinc

No evidence was found in the literature reviewed to indicate that inhalation, ingestion, or parenteral administration of zinc induces the formation of tumors. Based on the EPA carcinogenic classification system, zinc has a group D weight-of evidence, not classifiable as to human carcinogenicity. Wallenius et al. (1979) found that 4-nitro-quinoline-n-oxide-induced cancer of the oral cavity in female rats appeared earlier in animals ingesting a diet containing 200 mg/kg zinc than animals fed 15 or 50 mg/kg zinc. Another researcher discovered that a zinc-deficient diet (7

mg/kg) promoted the formation of methylbenzylnitrosamine-induced esophageal tumors (Fong et al., 1978).

2.3.3 Interaction with Other Compounds

Zinc oxide fumes have been reported to cause hypocalcemia in workers exposed at a zinc oxide factory (Klucik and Koprda, 1979). The range of employee exposure was 0.5 to 7.15 mg/m^3. Mulhern and co-workers (1986) reported that excess dietary zinc (2000 ppm zinc/day) produced copper deficiency in the offspring of C57 BL/GJ mice. The development of alopecia was also noted in the offspring by five weeks of age.

2.4 COPPER

Copper (Cu) is an essential element that occurs naturally in the +1 and +2 valence states. The biological availability and toxicity of copper are thought to be related to free Cu^{+2} ion activity (U. S. EPA, 1987b). Emissions of copper occur from natural (windblown dust, volcanoes, vegetation, forest fires, and sea spray) and anthropogenic sources (Nriagu, 1979). The valence state of copper emissions from iron and steel production is not known.

2.4.1 Noncancer Health Effects

The primary manifestations of exposure to copper fumes, dusts, or mists are dermatologic and respiratory symptoms (U. S. EPA, 1987b). "Metal fume fever" has been reported to occur following exposure to fine copper dusts (Gleason, 1968), copper fumes (Armstrong et al., 1983), and copper oxide and copper acetate dusts (Stokinger, 1981; Cohen, 1974). Copper concentrations as low as 0.1 mg/m^3 are reported to cause this disease (Gleason, 1968).

Human studies have been conducted to determine the chronic effects of copper exposure. Chronic effects observed for occupational exposure to copper

include contact dermatitis (Stokinger, 1981; Cohen, 1974; Williams, 1982) and leukocytosis (Armstrong et al., 1983). Mild anemia was reported by Finelli et al. (1984) in workers exposed to 0.6 to 1.0 mg/m^3 copper. Enterline and co-workers (1986) examined the overall mortality of 14,562 workers from the copper and zinc smelting industries and found no increased mortality. Plamenac et al. (1985) found that copper sulfate affected the respiratory epithelium and the pulmonary parenchyma.

In an animal study conducted by Johansson et al. (1984), 0.6 mg/m^3 copper chloride administered to rabbits 6 hours/day, 5 days/week for 4 to 6 weeks showed no significant changes in phospholipid content or histological lesions in the lungs of exposed rabbits. The only significant change observed was an increase in the number of alveolar type II cells. Another study, conducted by Lundberg and Camner (1984) and using the same concentrations and exposure times listed above, resulted in no observed changes in the number of alveolar macrophages or the lysozyme concentration in lavage fluid.

These data indicate that the unadjusted LOEL for humans exposed to copper and laboratory animals exposed to copper chloride is 0.6 mg/m^3. The investigations presented do not allow the estimation of a NOEL in either humans or laboratory animals.

2.4.2 Carcinogenicity of Copper

There is no available evidence to indicate that copper exposure can cause cancer (U. S. EPA, 1987b). Studies concerning the carcinogenicity, mutagenicity, and teratogenicity of inhaled copper or copper compounds could not be located in the available literature. As a result, the U. S.

Environmental Protection Agency has assigned copper to Group D, not classifiable as to human carcinogenicity.

2.5 NICKEL

Nickel emitted from steel mills is thought to be in the form of complex oxides of nickel and other metals (Page, 1983; Koponen et al., 1981). The following discussion includes any specific information found in the literature on chronic inhalation studies with nickel oxide. Where these data are lacking, the general effects of the nickel ion and other nickel compounds are presented.

2.5.1 Noncancer Health Effects

The direct respiratory effects of nickel compounds include asthma, nasal septal perforations, chronic rhinitis, and sinusitis (U. S. EPA, 1986a). Human exposure information for nickel is derived from occupational studies, and the literature reviewed contained no specific human data on the respiratory effects of nickel oxide. Asthma has been seen following working exposure to nickel carbonyl (Sunderman and Sunderman, 1961), and nickel sulfate exposure has resulted in septal perforation, chronic rhinitis, and sinusitis (Kucharin, 1970).

Respiratory effects studies of animals indicate that the nickel ion affects the viability and phagocytic activity of alveolar macrophages, and thus may affect resistance to respiratory infection (Graham et al., 1975a,b). Rabbits exposed to 1 mg/m^3 of metallic nickel dust for 3 and 6 months showed changes in the number and volume of alveolar epithelial cells, and the 6-month exposure group showed pneumonia (Johansson et al., 1981). Adult Wistar rats exposed to 25 ug Ni/m^3 for 4 months showed a significant increase in the size

and number of polynucleated macrophages and a 130% increase in phagocytic activity (Spiegelberg et al., 1984).

Studies of nickel effects on other systems are not well documented. Animal studies indicate that the nickel ion may affect carbohydrate metabolism (U. S. EPA, 1986a). Nickel has been shown to have low neurotoxic potential (NIOSH, 1977).

On the basis of the studies reviewed by the U. S. EPA (1986a), the increase in the size and number of polynucleated macrophages and increase in phagocytic activity in rats following 4 months of exposure to 25 ug/m^3 is estimated to represent the LOEL for exposure to nickel.

2.5.2 Carcinogenicity of Nickel

None of the three carcinogenic nickel compounds are known to be emitted from steel mills. These compounds are nickel refinery dust (Group A), nickel subsulfide (also Group A because it is the major species in refinery dust), and nickel carbonyl (Group B2, probable human carcinogen). The incremental unit risk due to lifetime exposure to 1 ug/m^3 is 2.4×10^{-4} for nickel refinery dust and twice that for nickel subsulfide (U. S. EPA, 1986a). The human evidence for nickel carbonyl's carcinogenicity is equivocal, but the presence of distal site tumors in animal studies implicate it as a Group B2 carcinogen (U. S. EPA, 1986a). No incremental unit risk has been calculated for nickel carbonyl.

Some studies indicate that the nickel ion may be the carcinogenic form, thus implicating all forms of nickel as potential carcinogens. Inhalation studies of nickel metal do not show the development of respiratory tract tumors, but one investigation found adenomatoid lung lesions in rats,

bronchial adenomatoid lesions in guinea pigs, an alveolar anaplastic carcinoma in one guinea pig lung, and a "metastatic lesion" in another animal (Hueper, 1958). This information (aside from the lack of controls in the guinea pig study), together with a strong tumor response from intramuscular injection (at the injection site), lends credence to the possibility that metallic nickel has limited evidence of carcinogenicity in animals (U. S. EPA, 1986a). Human epidemiologic studies of workers exposed to nickel metal are confounded by the presence of other possible carcinogens (U. S. EPA, 1986a).

2.5.3 Interaction with Other Compounds

Waalkes and co-workers (1985) reported that the injection of zinc offset renal damage and hyperglycemia seen in animals exposed to nickel. Pretreatment with nickel was shown to offset the effects of cadmium exposure in rats (Tandon et al., 1984).

2.5.4 Populations at Risk

Populations at special risk to adverse effects from nickel exposure are those with nickel hypersensitivity, generally from dermal exposures. While there is no information that nickel exposure of pregnant women leads to adverse effects, it has been shown that nickel can cross the placental barrier in animals (Stack et al., 1976).

2.6 CADMIUM

The toxicologic effects of cadmium exposure are important because the metal tends to accumulate and be retained in soft body tissues (especially in the kidneys); exposure occurs from ambient air, food, water, and from cigarette smoking; and the adverse health effects which occur following

exposure are generally irreversible (U. S. EPA, 1981). In addition, cadmium has been classified as a probable human carcinogen.

2.6.1 Noncancer Health Effects

Deposition following inhalation of cadmium is higher for smaller particles, and the absorbed cadmium is incorporated into metallothionein and deposited in the kidney (Task Group on Lung Dynamics, 1966). Chronic cadmium exposures thus typically result in renal dysfunction, which is the "critical" noncancer effect following cadmium exposure (Nordberg, 1976). Animal studies indicate a dose-related progression of kidney damage from early degenerative proximal tubule changes to interstitial edema and basement membrane fibrosis (U. S. EPA, 1981). Proteinuria is the biochemical index of renal dysfunction (U. S. EPA, 1981), and Kjellstrom (1976) estimated that workplace cadmium levels of 50 ug/m^3 increased the incidence of proteinuria in workers exposed for 10 to 20 years. The EPA (1981) estimated that industrial exposure for 10 years to cadmium levels of 23 to 25 ug/m^3 would result in renal cadmium levels sufficient to induce proteinuria.

The chief chronic pulmonary effect of cadmium exposure is centrilobular emphysema and bronchitis (U. S. EPA, 1981). These effects have been found following occupational exposure to cadmium-oxide fumes, cadmium-oxide dust, and cadmium-pigment dust (Friberg et al., 1974). Lung impairment has been seen in workers exposed to cadmium oxide levels below 100 ug/m^3, depending on exposure length (Lauwerys et al., 1974).

Several investigators have found that cadmium exerts immunosuppressive effects in animal studies (Koller et al. 1975, Cook et al., 1975a,b; Exon et al., 1975), but these effects have not been demonstrated in humans.

In order to estimate a NOEL and a LOEL for cadmium inhalation exposure, exposure from other routes must also be considered because of cadmium's accumulation and retention within the body. The U. S. EPA (1981) specified a critical cadmium renal cortex concentration for renal dysfunction, and assessed the impact of ambient air cadmium exposures taking into account differing dietary intake levels and smoking status. In general, the EPA (1981) concluded that ambient levels below 10 ng/m^3 do not significantly increase kidney cortex concentrations of cadmium, but above 100 ng/m^3 renal accumulation begins to occur and 1,000 ng/m^3 approaches the critical level for renal dysfunction. Thus, 10 ng/m^3 can be considered the NOEL for cadmium inhalation exposure, and 100 ng/m^3 the LOEL.

2.6.2 Carcinogenicity of Cadmium

Cadmium is listed by the EPA's HHAG as a B1 carcinogen (probable human carcinogen by inhalation). The basis for this classification is limited evidence from epidemiologic studies and sufficient evidence of carcinogenicity in two animal species (U.S. EPA, 1989).

Thun and co-workers (1985) studied the incidence of lung cancer among cadmium smelter workers, and reported a 2-fold excess risk of lung cancer. Like the other epidemiologic studies of cadmium-exposed workers (Varner, 1983; Sorahan and Waterhouse, 1983; Armstrong and Kazantzis, 1983), however, the presence of other carcinogens may have confounded the results. The U. S. EPA thus considers cadmium to have only limited evidence of human carcinogenicity (U.S. EPA, 1989).

Evidence of cadmium's carcinogenic potential in animal studies is based on increased lung tumors in rats exposed to cadmium and cadmium oxide via

inhalation (Takenaka et al., 1983), and injection site tumors in rats and mice following intramuscular and subcutaneous injection (U.S. EPA, 1989).

On the basis of these results, the EPA calculated a unit risk number of $1.8 \times 10^{-3}/ug/m^3$ for cadmium exposure. Thus, a person exposed continuously to 1 ug/m^3 of cadmium for life has a probability of getting lung cancer of not more than 1.8 chances in 1000. A conservative estimate is that a lung cancer risk of 1 in 10,000 would occur at a concentration of 0.06 ug/m^3 annual average cadmium (U.S. EPA, 1989).

2.6.3 Interaction with Other Compounds

Cadmium is affected by or can affect levels of other metals in the body. A deficiency of zinc increases the toxicity of cadmium, and increased zinc levels offset cadmium's toxic effects (Choudhury et al., 1977; Pond and Walker, 1975). Individuals with low iron levels may have a four-fold increase in cadmium absorption.

2.6.4 Populations at Risk

Populations especially at risk to cadmium exposure are the elderly (due to its long retention in the body), cigarette smokers, and those whose diets add high amounts of the metal. The reader should refer to the U. S. EPA (1981) document for detailed information on the estimated relative contribution of cadmium through diet, smoking, and ambient air exposures.

2.7 VANADIUM

Vanadium is a naturally occurring metal that is widely distributed in small amounts in the earth's crust. It is also found in trace amounts in fossil fuels (U. S. EPA, 1987c). Vanadium in the air is believed to be solely a result of industrial processes. The oxidation states of vanadium are +2,

+3, +4 and +5 (NLM, 1986). It could not be determined which species of vanadium are emitted from steel mills. The following discussion is focused primarily on the effects of vanadium pentoxide exposure because the literature contains little to no other information concerning inhalation exposures to vanadium or its salts.

2.7.1 Noncancer Health Effects

The chronic effects of various vanadium compounds have been studied in man with most reporting only minor irritations of the respiratory tract. Sjoberg (1950) evaluated 36 workers exposed to vanadium pentoxide (0.05-5.58 mg/m^3) at a vanadium processing plant in Sweden. Severe respiratory irritation was the most common manifestation found in the workers, whom the study followed for a two year period. In a study by Lewis (1959), 24 men exposed to vanadium pentoxide concentrations ranging from 0.018 to 0.38 mg/m^3 had an increased incidence of respiratory distress (cough, bronchospasm, pulmonary congestion). The average duration of worker exposure was 2.5 years and the author concluded that there were no permanent effects from chronic vanadium exposure. Other chronic manifestations reported in the literature include conjunctivitis, tracheobronchitis, and contact dermatitis (Tebrock and Machle, 1968; Symanski, 1939).

Subchronic effects resulting from relatively high concentrations of vanadium have also been reported. A number of studies have documented the development of respiratory symptoms (wheezing, coughing, dyspnea) after exposure to high concentrations of vanadium over short time periods (Musk and Tees, 1982; Zenz et al., 1962; McTurk et al., 1956). Zenz and Berg (1967) exposed 2 volunteers to 1 mg/m^3 vanadium pentoxide for 8 hours and reported

the presence of persistent cough in both. These investigators also exposed 5 other volunteers to 0.2 mg/m^3 of vanadium pentoxide for 8 hours and reported the development of a cough that lasted from 7 to 10 days. The unadjusted LOEL based upon the above human studies would be 0.018 mg/m^3 for vanadium pentoxide. A NOEL could not be determined from the data.

2.7.2 Carcinogenicity of Vanadium

The available literature on vanadium is not sufficient to evaluate its carcinogenicity in laboratory animals or man. As a result, EPA has classified vanadium a Group D carcinogen, not classifiable as to carcinogenic potential.

2.7.3 Interaction with Other Compounds

Vanadyl sulfate (25 ppm) has been found to inhibit the carcinogenic effects of 1-methyl-1-nitrosourea in rats (Dimond et al., 1963). In terms of antidotes, ascorbic acid and ethylenediaminetetraacetate were effective in sequestering vanadium poisoning in mice, rats and dogs (Mitchell and Floyd, 1954).

3.0 HEALTH EFFECTS OF OTHER COMPOUNDS EMITTED FROM STEEL MILLS

3.1 AMMONIA AND AMMONIUM SULFATE

This section discusses the health effects associated with exposure to ammonia and ammonium sulfate. Both of these compounds are known to be emitted from steel mill operations (Barnard, 1989).

3.1.1 Noncancer Health Effects

Exposure to ammonia will cause rapid increases in blood ammonia concentrations, as it is readily absorbed through the lungs (U. S. EPA, 1988). The U. S. Environmental Protection Agency (1986b) reported that no adequate animal studies with chronic exposures were found in the literature. Similarly, the available human chronic exposure information is limited. The available subchronic animal information and the human exposure information as presented by the EPA (1988) are summarized below.

The National Research Council (1977) reported the average odor threshold for ammonia to be 5 ppm (3.5 mg/m^3). Continuous exposure to ammonia may cause an increase in the occurrence or severity of respiratory tract infections (National Research Council, 1977). Retention of ammonia in the respiratory tract is about 80 percent for humans (not dose-related) (Silverman et al., 1949).

No clinically significant effects were seen in one study of rats, guinea pigs, rabbits, dogs, or monkeys exposed continuously to 57 ppm (40 mg/m^3) ammonia for 114 days (Coon et al., 1970). Mice and guinea pigs exposed to 20 ppm (14 mg/m^3) for 28 days also showed no effect (Anderson et al., 1964), but no exposure time was given. However, when exposure duration was increased to 42 days or concentration was increased to 50 ppm (35 mg/m^3), pulmonary edema,

congestion, and hemorrhage occurred (Anderson et al., 1964). These studies considered the lowest observed effect levels (14 mg/m^3 for 42 days and 35 mg/m^3 for 28 days) and the no observed effect level (14 mg/m^3 for 28 days) as presented by the U. S. EPA (1986b). The limited data available and the fact that these studies are based on subchronic rather than chronic exposures make it difficult to conclude that these are the true NOELs and LOELs.

Chronic exposure to humans at 30 mg/m^3 ammonia caused headaches, nausea, and reduced appetite (National Research Council, 1977), but again no averaging time was reported. Repeated exposure to 17, 35, or 69 mg/m^3 for 6 hours per day per week, for 6 weeks showed no changes in respiratory rate, blood pressure, pulse, or forced vital capacity, but mild eye irritation occurred in the early sessions (Ferguson et al., 1977).

In its review of the health effects of acid aerosol exposure, EPA found that most of the studies of acid aerosols involve sulfuric acid, but some effects of ammonium sulfate [$(NH_4)_2SO_4$] can be inferred from these studies (U.S. EPA, 1988). Most of the studies of acid aerosol exposure to humans do not involve ammonium sulfate, and the only studies described by the Environmental Protection Agency (1988) involved short exposure durations. One study showed no effects in asthmatic and normal human subjects exposed to up to 1.0 mg/m^3 (0.5-1.0 mass median aerodynamic diameter, MMAD) for 16 minutes (Utell et al., 1982).

The LOAEL based on animal studies reviewed by the Environmental Protection Agency (1988) was determined from a study by Godleski et al. (1984) in which emphysemic lesions were seen in hamsters exposed to 187 ug/m^3 (0.187 mg/m^3) $(NH_4)_2SO_4$ (0.3 MMAD) for 6 hours per day, 5 days per week, for

15 weeks. Busch et al. (1984) found interstitial thickening in rats and guinea pigs exposed to 1.03 mg/m^3 $(NH_4)_2SO_4$ (0.42 MMAD) for 6 hours/day, 5 days/week, for 20 days. Other studies of ammonium sulfate exposure were based on short term exposures (usually 1 hour) to 0.4 to 9.54 mg/m^3 (Amdur et al., 1978; Loscutoff et al., 1985; Schlesinger et al, 1978).

3.1.2 Carcinogenicity of Ammonia and Ammonium sulfate

No inhalation information is available to assess the carcinogenicity of ammonia, but it has been shown to be noncarcinogenic in mice following oral administration (Toth, 1972; Uzvolgi and Bojan, 1980). The EPA's HHAG considers ammonia a group D compound, with insufficient evidence to judge its carcinogenic potential in humans. No discussion of ammonium sulfate's carcinogenic potential is provided by the Environmental Protection Agency (1988), and this pollutant is not currently included in the IRIS data base.

3.1.3 Interaction with Other Compounds

The effect of ammonium sulfate exposure in conjunction with exposure to other pollutants has been examined. Exposure to 2.6 mg/m^3 SO_2 and 528 ug/m^3 $(NH_4)_2SO_4$ in human subjects for 4 hours showed upper airway irritation in 9 of 20 subjects, as compared to 4 of 20 subjects receiving SO_2 exposure only (Kulle et al., 1984). Acid aerosols of ammonia have also been shown to provide short-term protection (up to 6 months) against benzo(a)pyrene-induced tumors (Godleski et al., 1984).

3.2 HYDROGEN CHLORIDE

Hydrogen chloride (hydrochloric acid) is an acutely toxic gas because it is highly soluble in water, and the resulting hydronium ion is reactive with organic molecules and causes cellular injury and necrosis (U. S. EPA, 1987d).

The World Health Organization (WHO, 1982) reports a threshold for odor perception of 0.2 ppm (0.3 mg/m^3), but other reports range from 0.1 to 459 mg/m^3 (U. S. EPA, 1987d).

3.2.1 Noncancer Health Effects

There are little chronic or subchronic inhalation data available for hydrogen chloride in the literature. One subchronic study of guinea pigs exposed to 0.15 mg/m^3 hydrogen chloride for 2 hours/day for 28 days showed no effect (Kirch and Drabke, 1982). Guinea pigs exposed to 15 mg/m^3 for 2 hours/day, 5 days/week for 49 days showed no differences in lung function compared to controls (Oddoy et al., 1982).

The only chronic study of hydrogen chloride exposure evaluated the effects of inhalation of 15 mg/m^3 on Sprague-Dawley rats exposed for 6 hours/day, 5 days/week for life (Albert et al., 1982). Nasal mucosa lesions found at autopsy included rhinitis, epithelial or squamous hyperplasia, and squamous metaplasia. Because of the limited data available, 15 mg/m^3 hydrogen chloride can be considered the LOAEL, and a NOAEL of 0.15 mg/m^3 can be estimated from the subchronic hamster study of Kirche and Drabke (1982).

3.2.2 Carcinogenicity of Hydrogen chloride

There are no adequate epidemiologic or animal carcinogenicity studies of hydrogen chloride, thus it is classified as a Group D carcinogen.

3.3 TOLUENE

Toluene, another compound that may be emitted during the steel-manufacturing process, has its primary effects on the central nervous system, with occupational studies reporting symptoms of headache, dizziness, fatigue and feelings of intoxication among those exposed. Gusev (1965) estimated the

minimum toluene odor threshold to be 0.40 to 0.85 ppm (1.5 to 3.2 mg/m^3). May (1966), however, found the minimum odor threshold to be 37 ppm (140 mg/m^3).

3.3.1 Noncancer Health Effects

Several investigators (Anderson et al., 1983; Baelum et al., 1985; Ogato et al., 1970; von Oettingen et al., 1942) evaluated the effects of toluene in workers exposed for 1 day to concentrations of 0, 10, 40, 100, and 200 parts per million (ppm). At 100 ppm (377 mg/m^3), nasal and eye irritation, headache, dizziness, and intoxication were reported among those exposed for 6 hours (Andersen et al., 1983). Groups exposed for 6 hours to 10 and 40 ppm (38 and 151 mg/m^3) reported no effects. Baelum and co-workers (1985) also found neurotoxic effects in workers (with a history of toluene exposure) exposed to 100 ppm for 6.5 hours.

Ogata and co-workers (1970) examined subjects exposed to 200 ppm (754 mg/m^3) for 7 hours and found prolongation of reaction time and decreased pulse rate. Dr. von Oettingen et al. (1942) reported that muscular weakness, confusion, and impaired coordination occurred following exposure to 200 ppm for 8 hours, and at 100 ppm moderate fatigue and headache occurred. Wilson (1943) reported headaches and lassitude among humans exposed for 1 to 3 weeks to 50 and
100 ppm toluene.

On the basis of these 1-day occupational studies, it can be concluded that the LOAEL for toluene exposure is 100 ppm (377 mg/m^3) and the NOAEL is 40 ppm (151 mg/m^3). This information has strong support even though the studies are based on one-day exposure periods. This support includes longer-term animal studies such as those of the American Petroleum Institute (1980),

Gibson and Hardisty (1983), Kyrklund et al. (1987), and Okeda et al. (1986). The American Petroleum Institute (1980) conducted a chronic rat study for 26 weeks with exposure levels of 0, 100, and 1500 ppm for 6 hr/day, 5 days/week. The LOAEL for this study was 100 ppm. Gibson and Hardisty (1983) exposed rats to 0, 30, 100 and 300 ppm for 6 hr/day, 5 days/week for up to 24 months, and reported a LOEL of 100 ppm.

3.3.2 Carcinogenicity of Toluene

Toluene's carcinogenic potential has been evaluated by the National Toxicology Program (U. S. DHHS, 1989). Toxicology and carcinogenesis studies in rats and mice exposed to toluene by inhalation for 15 or 24 months (0, 600, and 1200 ppm) indicated no evidence of carcinogenicity (U. S. DHHS, 1989). The Chemical Industry Institute of Toxicology (1980) also concluded that exposure to toluene levels of 30, 100 and 300 ppm for 24 months did not implicate toluene as a carcinogen. As a result, the U. S. Environmental Protection Agency has assigned toluene to Group D, not classifiable as to human carcinogenicity.

3.4 BENZENE

Benzene is an aromatic hydrogen that is slightly soluble in water. Once a widely used solvent, benzene can produce narcotic effects similar to those of toluene. Of most concern, however, are the hematotoxic effects of benzene.

3.4.1 Noncancer Health Effects

Deichmann and co-workers (1963) studied the effects of subchronic benzene inhalation exposure in rats at concentrations ranging from 15 to 83 ppm (48 to 2600 mg/m^3). Groups exposed to 47 and 44 ppm (150 and 140 mg/m^3) for 7 hours/day, 5 days/week for 8 weeks or more showed slight or moderate

leukopenia. Groups exposed to ≤ 31 ppm (99 mg/m^3) showed no effects, and this level is reported by the EPA (1984c) to be the NOEL for leukopenia in rats.

Chronic mouse inhalation studies conducted by Snyder et al. (1980) revealed marked lymphocytopenia, slight anemia, and bone marrow hypoplasia in mice exposed to 100 ppm (320 mg/m^3) benzene for 6 hours/day, 5 days/week for life. Chronic human exposure to benzene may cause pancytopenia (a reduction in blood erythrocytes, leucocytes, and thrombocytes)(U. S. EPA, 1984c). Mild cases of anemia, leukopenia, and thrombocytopenia are generally reversible if exposure is ceased. Studies by NIOSH (1974) indicate that the lowest limit of hematologic effects in humans is less than 100 ppm (Hardy and Elkins, 1948; Pagnotto et al., 1961). Elkins (1976) and Pagnotto et al. (1977) conclude that a benzene level of 25 ppm (80 mg/m^3) is safe for most workers.

3.4.2 Carcinogenicity of Benzene

There is substantial evidence from epidemiologic studies that benzene causes leukemia (U. S. EPA, 1985). Benzene is thus a Group A known human carcinogen. Animal studies have not demonstrated this effect, however. Epidemiologic studies by Pinsky et al. (1981), Ott et al. (1978), and Wong et al. (1983) were reviewed by the U. S. EPA (1985) in order to prepare an inhalation unit risk estimate of $8.3 \times 10^{-6}/ug/m^3$ for benzene. This can be translated to indicate that a person's risk of getting lung cancer, following continuous lifetime (70 years) exposure to 1 ug/m^3 of benzene will not exceed 8.3 chances in one million.

3.4.3 Interaction with Other Compounds

The metabolism and toxicity of benzene can be affected by the presence of other solvents that are oxidized by the same hepatic enzymes (Ikeda et al.,

1972). These solvents include xylene and toluene. The inability of benzene alone to induce leukemia in experimental animals has lead some researchers to hypothesize that the hematotoxic effects seen in humans are actually the result of exposure to benzene along with other solvents. (Andrews et al., 1977; U. S. EPA, 1980).

3.5 NAPHTHALENE

Naphthalene is an aromatic hydrocarbon that can be released to the ambient environment either in a gaseous or particulate form. While airborne, naphthalene will undergo photochemical degradation and has a half-life of eight hours during sunlight hours. At night, it has been estimated that naphthalene has a half-life of 15 hours as a result of reaction with nitrate radicals (U. S. EPA, 1987e).

3.5.1 Noncancer Health Effects

The health effects associated with inhalation exposure to naphthalene have not been well documented in either humans or laboratory animals (U. S. EPA, 1987e). Cataracts have been found to develop in individuals exposed to naphthalene by the oral, dermal, and inhalation routes (U. S. EPA, 1980). Naphthalene exposure in the occupational setting also has resulted in cataract development (Ghetti and Mariani, 1956; Hollowich et al., 1975). Acute effects of naphthalene exposure have been reported in humans, the most common manifestation being acute hemolytic anemia. Investigators have described incidences where acute hemolytic anemia has developed after combined dermal absorption and inhalation of naphthalene vapors by neonates (Grigor et al., 1966) and adults (Younis et al., 1957), and inhalation of naphthalene vapors alone by neonates (Hanssler, 1964) and adults (Linick, 1983). The

concentration of the naphthalene in the above cases was not reported in the literature due to the poorly defined nature of the exposure.

Few studies have been conducted on laboratory animals to determine the effect of naphthalene exposure. An 8-hour Median Lethal Concentration (LC_{50}) value of 180 ppm (940 mg/m^3) for naphthalene in laboratory animals was reported by Union Carbide (1968). However, Buckpitt (1985) suggests that this value may be too low based on the oral and intraperitoneal Median Lethal Dose (LD_{50}) values. Male and female Wistar rats exposed to 78 ppm (408 mg/m^3) naphthalene for 4 hours resulted in no mortalities, nor any lung, liver, kidney or nasal passage abnormalities (Fait and Nachreiner, 1985). This value, 78 ppm naphthalene, could be considered the unadjusted NOEL in laboratory animals. In an unpublished inhalation study by Buckpitt (1985), male Swiss-Webster mice were exposed to 90 ppm (470 mg/m^3) naphthalene for 4 hours without any resulting mortalities. The researcher did note the development of prominent lesions in the lungs of the exposed mice, however. This value reported by Buckpitt, 90 ppm naphthalene, is the unadjusted LOEL in laboratory animals.

3.5.2 Carcinogenicity of Naphthalene

Because of the lack of definitive data, naphthalene is classified as a Group D carcinogen. The available evidence is inadequate to evaluate the carcinogenic potential of naphthalene in man.

4.0 HEALTH EFFECTS OF COMPLEX MIXTURES

Sections 2.0 and 3.0 of this report presented health effects information for individual pollutants that comprise steel mill emissions. This section discusses the effects of mixtures known to be emitted during steel manufacture. Polycyclic organic matter is one such mixture, and denotes many chemical groups, including polycyclic aromatic hydrocarbons, aza-, imino-, and carbonyl-arenes, and polychloro compounds, among others.

The coke oven emission mixture includes not only polycyclic organic matter, but also includes many of the individual pollutants discussed in Sections 2.0 and 3.0. These pollutants include cadmium, chromium, nickel, ammonia, toluene, and benzene.

4.1 POLYCYCLIC ORGANIC MATTER

Polycyclic organic matter (POM) is a mixture of many groups of compounds commonly formed in combustion or high temperature processes involving carbon and hydrogen (Santodonato et al., 1979). The two POM groups most commonly detected in ambient air are polycyclic aromatic hydrocarbons (PAH) and PAH nitrogen analogs (aza- and imino- arenes). Polycyclic organic matter is generally present in the atmosphere as particulate matter or attached to particulate matter.

4.1.1 Noncancer Health Effects

Benzo(a)pyrene (BaP) is the best known and most studied PAH, and much of the POM health effects knowledge is derived from BaP studies. The major health-related effects of POM inhalation involve local lesions of the respiratory tract (Santodonato et al., 1979). Particle size of the POM or POM carrier is very important in determining deposition, cellular reactions, and

clearance of inhaled POM. Mucociliary clearance plays an important role in the reactivity and clearance of POM. Scala (1975) has shown that irritants that inhibit ciliary activity can increase the length of time POM is present in the tracheobronchial tract, thus increasing the potential to form reactive electrophiles. These reactive electrophiles are capable of interacting with cellular constituents such as RNA, DNA, and proteins, which can lead to the formation of tumors (Lehr et al., 1978). This process will be covered in more detail in Section 4.1.2. Tumor formation is also possible due to particles that are cleared via mucociliary activity, swallowed, and absorbed through the gastrointestinal tract (Santodonato et al., 1979)

There is little information in the literature on the noncancer health effects of POM. Several POM are known to be noncarcinogens (i.e., benzo(e)pyrene, anthracene). Several POM have been shown to be immunosuppressives (Malmgren et al., 1952), but immunosuppression is thought to be correlated with carcinogenic potency (Baldwin, 1973). Benzo(e)pyrene and anthracene show no immunosuppression.

Other noncancer effects occur associated with exposure to carcinogenic POM. Gross and co-workers (1965) administered 100 ug of 7-12 dimethylbenz(a)anthracene (DMBA) or BaP via intratracheal application to hamsters for 4 to 16 months that resulted in acute pneumonia and chronic pneumonitis.

Because of the complexity of the POM mixture and the lack of noncancer data in the literature, it is not possible to delineate NOEL or LOEL values. It is thought, however, that the noncarcinogenic effects of POM will occur at the same dose levels that induce tumor formation.

4.1.2 Carcinogenicity of Polycyclic Organic Matter

There is little quantitative cancer data available for POM. Most of the information available concerns PAH compounds. Benzo(a)pyrene, benz(a)anthracene, dibenzo(a,h)pyrene, dibenz(a,h)anthracene, and dibenzo(a,i)pyrene are considered animal carcinogens. Benzo(a)pyrene and dibenz(a,h)anthracene are complete carcinogens (capable of initiation and promotion), and have similar carcinogenic potency (Santodonato et al., 1979). Benz(a)anthracene, dibenzo(a,i)pyrene, and dibenzo(a,h)pyrene are weaker carcinogens (Santodonato et al., 1979).

Benzo(a)pyrene is the only POM included in IRIS with quantitative carcinogenic information, and it is classified as a B1 probable human carcinogen (U.S. EPA, 1989). The human data are inadequate to judge BaP's ability to induce cancer because BaP cannot be delineated as the cancer causing agent in studies of cigarette smoke, roofing tar, and coke oven emission exposures.

Benzo(a)pyrene has sufficient evidence as an animal carcinogen, with subcutaneous, intramuscular, intratracheal, and oral administration resulting in tumors in mice, rats, rabbits, and hamsters (U.S. EPA, 1989). Inhalation of BaP at concentrations of 2.2, 9.5, and 45 mg/m^3 for up to 24 months in hamsters resulted in respiratory tract tumors in the groups exposed to 9.5 and 45 mg/m^3 (Thyssen et al., 1981). Based on this study, the unit risk number for BaP is calculated to be $1.7 \times 10^{-3}/ug/m^3$.

4.2 COKE OVEN EMISSIONS

Coke is used primarily in the steel industry's blast furnaces to generate iron which is subsequently refined into steel (U. S. EPA, 1984d).

During the production of coke, chemically-complex emissions are released which consist of gases and respirable particulate matter. An extensive list of these emissions can be found in the EPA document "Carcinogen Assessment of Coke Oven Emissions" (U. S. EPA, 1984d).

4.2.1 Noncancer Health Effects

The available literature on the effects of coke oven emissions focuses on coal tar, which results from the condensation of coke oven emissions. Kinkead (1973) exposed Sprague-Dawley yearling rats, Sprague-Dawley weanling rats, ICR mice, and CAF-1 mice to an aerosol of coal tar continuously for 90 days at concentrations of 0.2, 2.0, and 10 mg/m^3. The result was a high degree of mortality among the exposed animals attributable to general debilitation resulting in greater chance of infection. A high incidence of chronic murine pneumonia was observed in all species studied (Kinkead, 1973).

In another study, MacEwen and co-workers (1976) investigated the effect of a coal tar mixture collected from multiple coke ovens in the greater Pittsburgh area. ICR-CF-1 mice, CAF-1-JAX mice, weanling Sprague-Dawley rats, New Zealand white rabbits, and Macaca mullata monkeys were exposed to a coal tar aerosol at 10 mg/m^3, 6 hour/day, 5 days/week, for 18 months. The investigators reported a significant inhibition of body growth rate in the rabbits after 1 month and in the rats after 4 months. None of the monkeys showed significant inhibition of growth (MacEwen et al., 1976).

On the basis of these animal studies, an unadjusted LOAEL of 0.2 mg/m^3 can be estimated for exposure to coke oven emissions (coal tar).

4.2.2 Carcinogenicity of Coke Oven Emissions

A large body of literature exists concerning the carcinogenic activity of coke oven emissions in humans. In a review of the available epidemiologic literature by the U. S. EPA (1984d), it was concluded that exposure to coke oven emissions increases the risk of lung, tracheal, bronchial, kidney, and prostrate cancer, as well as cancer at all sites combined. Redmond et al. (1972, 1976, 1979) conducted a number of epidemiologic studies to determine if coke oven emissions result in increased cancer risk. In the 1979 study this group found a significant excess of lung, trachea, and bronchus cancer mortality in coke oven workers. The investigation also showed an increase in prostate and kidney cancer (Redmond et al., 1979). Lloyd (1971) found an increase in death from respiratory neoplasms and an increase in mortality from all causes in steelworkers employed in 1953 in the coke plants of two Allegheny County, Pennylvania steel mills.

Animal models have also been used to assess the carcinogenic potential of coal tar. C3H mice were exposed to 0.30 mg/liter coal tar aerosol for 2-hour periods, 3 times a week for up to 36 weeks (Horton et al., 1963). Six of the 33 mice tested developed squamous cell tumors in the periphery of the lung. Tye and Stemmer (1967) studied the carcinogenic effects of different fractions of coal tar in male C3H/HeJ mice. The mice were exposed to 0.20 mg/liter for 2 hours every 3 weeks during the first 8 weeks, but, because so many mice died during this time period, the concentration was reduced to 0.12 mg/liter for the remainder of the experiment (55 weeks). Upon histological examination, adenomas and adenocarcinomas of the lung were observed in 60 to

100% of the mice inhaling aerosols of coal tars while control mice developed no observable tumors.

The available epidemiologic and animal data overwhelmingly prove that coke oven emissions are carcinogenic in man and experimental animals. Three separate organizations have classified the coke oven emission mixture as a known human carcinogen. The U. S. EPA lists coke oven emissions as a Group A carcinogen; the International Agency for Cancer Research groups coke oven emissions into category 1; and the National Toxicology Program also classifies coke oven emissions as a known human carcinogen. The EPA's unit risk number for coke oven emissions, based on lifetime continuous exposure to 1 ug/m3 Benzene Soluble Organics (BSO), is $6.2 \times 10^{-4}/ug/m^3$, based on epidemiologic studies of steelworkers exposed to coke oven emissions for up to 15 years.

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